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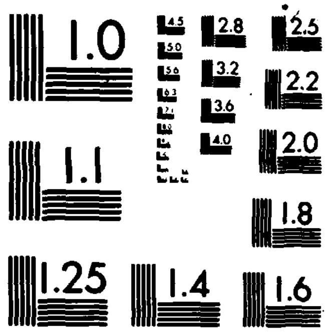

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19. ABSTRACT (Continue on reverse if necessary and identify by block number)

The [illegible] of this project is to measure the brain's magnetic field, and use these data [illegible] late sources of fields within the brain that are differentially affected by w[illegible] attention. A subsidiary goal is to determine if multiple or single sources u[illegible] ponents of the event related potential, and to locate these sources. During the [illegible] report period progress was made in instrumentation, data handling, and in [illegible] involving [illegible] activity which was differentially affected [illegible] the state of [illegible] of the subject. Modifications or our primary sensing system permitted an improvement in the signal-to-noise ratio by a factor of four. Experiments with this system had a major impact on the design of a multi-sensor array, which will be used on this project this year. A scanner for mapping the field about the head was designed and constructed. Software for handling multi-channel information was created. A means for communicating with a CYBER and a VAX computer for handling large amounts of data was implemented. Experiments revealed that visual attention to a stimulus caused a [illegible]

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19. modulation in background brain activity from the visual cortex at the onset of a 100 msec component of the event related potential. The duration of the modulation depended upon the level of attention. A late 400 msec component in the event related potential has a cortical source in the temporal region. However, the 200 and 300 msec components have deep subcortical sources. Differences in response based on modality and nature of the task are still being studied.

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NEUROMAGNETIC INVESTIGATION OF WORKLOAD AND ATTENTION

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ANNUAL TECHNICAL REPORT

AFOSR Contract No. F49620-82-K-0014

Submitted by New York University

INTRODUCTION

This annual technical report describes the progress we have made in studying "The Effects of Workload and Attention on the Neuromagnetic Response." Using a system based on the Superconducting Quantum Interference Device (SQUID), we are able to detect extremely weak magnetic fields associated with the flow of electric current in the human brain. Because of unique features of this method, it is possible to sharply localize the source of the field. In fact, the starting point of this project was our success in locating the source of the 'P300' component of the Event Related Potential (ERP) in or near the hippocampal formation. This led to an attempt to identify cortical sources of components of the ERP, and to determine whether the variation in activity of sources that contribute to the ERP varies differentially with the nature of the task required of the subject, as well as his or her state of attention. We have made progress on several fronts during this project. This report will describe developments in several areas, and indicate how they relate to the overall goals of the project.

I. TECHNICAL DEVELOPMENTS

1. Modifications to the Basic System

During the first year of the project we worked with a magnetic sensing system based on the rfSQUID. During that time the S.H.E. Corp. announced a commercial version of a dcSQUID which provides an improvement of an order-of-magnitude in intrinsic SQUID noise. Of course, noise due to other components of the system also contribute, but by incorporating a dcSQUID, as well as other changes, e.g., to the rf shield, we anticipated a gain in signal-to-noise by a factor 4. These modifications were made, and after extensive tests we found that the upgraded system had a white-noise level of 20 fT per root Hertz, which is a factor of 4 better than the prior system. This made it possible for us to obtain more reliable measures of fields associated with the ERP. It also allowed us to make some tests that affected the design of the multi-sensor array to be described below.

In one of these tests we used an rfSQUID to sense the ambient noise, and used this noise to cancel correlated 1/F noise sensed by the dcSQUID. This test was necessary to determine if it is feasible to reduce the 1/F noise (which becomes appreciable below about 1 Hz in the dcSQUID system). Since many of the ERP components of interest have significant low-frequency content (and are distorted by filter cut-offs of 0.5 Hz or higher), it is of some importance to reduce the low-frequency 1/F noise. This cancellation procedure was found to be highly effective, and we decided to incorporate it in the multi-sensor array.

2. The Multi-Sensor Array

With funding from the Office of Naval Research, we worked with S.H.E. Corp. scientists in developing a prototype system that includes 5 channels based on dcSQUIDs, plus 4 rfSQUID channels for sensing the ambient field for purposes of noise reduction. Three of the rfSQUIDs are configured as magnetometers and sense field in the X, Y and Z directions. The fourth rfSQUID is part of a first-order gradiometer system to sense the field gradient in the Z-axis. These four outputs, together with their time-derivatives, will be given optimum weightings before being used to cancel noise in the active channels (second order gradiometers coupled to dcSQUIDs). The system has undergone preliminary tests at S.H.E. Corp. and meets all specifications. We expect to take delivery within the next 7 days.

While ONR covered the cost of this system and associated electronics, we expended considerable effort on the present program in conducting preliminary tests, designing and constructing a flexible holder for positioning the large dewar and for scanning the head, and in preparing software for the use of the system in this workload study. The scanner is now completed and is in the laboratory awaiting the multi-sensor system. It is being oufitted with stepping motors so that ultimately it can be placed under computer-control for scanning the head. One of the main justifications for this extensive effort is that repeated measurements from about 80 positions

about the head were required to map the field pattern associated with the P300 component. This was an extremely time-consuming task. Moreover, even in a simple odd-ball experiment it is difficult to assure that the subject's response would remain stable over many hundreds of repeated trials. Since there will be five active channels in the new system, it should be possible to map the field much more quickly, and require far fewer trials. Also the enhanced signal-to-noise ratio will allow us to use fewer replications. In effect, there is a built in replication because of the configuration of pick-up coils, which will allow us to keep a coil over one spot while the other four coils are moved to new spots.

The five channels for measuring fields from the brain, as well as 8 channels of ambient field data for cancellation of noise by software, required us to develop an extensive package of computer programs over the past few months. In addition, the amount of data we will have to analyze will be truly enormous, so arrangements were made to allow our PDP11/34 computer to communicate with the mainframe CYBER computer or with one of the VAX computers at the Courant Institute. This computer time will be provided at no-cost to the project, and it will facilitate the extensive "number crunching" that will be associated with every experiment. With all of this preparatory work completed or nearing completion, it should require a minimum amount of time to get the new system up and running.

II. EXPERIMENTAL RESULTS

1. Modulation Studies

In 1970 Kaufman and Locker reported that EEG activity is modulated in-step with event related potentials. Also, Spekreisje and Reits (1980) demonstrated the presence of sidebands in the EEG spectrum during sensory stimulation. These sidebands must result in modulation of the EEG.

The modulation of the EEG by event related potentials is bound to occur if spontaneous EEG activity and evoked activity occur together in the same (nonlinear) neural structures. Since evoked cortical activity is often at twice the frequency of any simple harmonic input, cortical neural networks must often exhibit essential nonlinearities.

It is important to recognize that the averaging computer is a comb filter, in the sense that it enhances harmonics of the fundamental stimulus frequency and attenuates the background "noise". Thus, all commponents of the EEG that are not time-locked to a stimulus event are attenuated as noise. This would include all of the sidebands resulting from any interaction of the evoked activity and the ongoing EEG. Hence, valuable information may be discarded along with noise during the signal averaging process. This information may well complement the N100, P300 amd N400, as well as other components of the ERP that reflect mental activity of different kinds.

The fact that alpha blockage occurs during visual attention is a strong indication that at least some type of change occurs in the spontaneous EEG. Existing theories of this blockage are based on the notion of "desynchronization", which suggests that normal alpha is attributable to a group of loosely coupled free-running oscillators, and these become uncoupled during attention, so that activity at alpha frequencies is effectively cancelled because the oscillations are out-of-phase with each other. An alternative view is that alpha activity occurring in cortical neurons is modulated because of non-linear interactions with other attention-related cortical events. While Kaufman and Locker demonstrated modulation of brain activity by steady state conditions, we focussed on its modulation by transient events -- events that are capable of evoking P300-like phenomena.

Before proceding with a sumnmary of our results to date, it is important to keep in mind the distinction between cortical EEG and components of the ERP, which may or may not have cortical sources. P300 appears to have a subcortical source, namely in the hippocampal formation. N100, which is also affected by cognitive factors, seems to have a cortical source, as does N400 (see below). Alpha blockage (which we do not consider to be a form of "desynchronization") is most likely to be related to modulation of activity of neurons in the visual cortex, and is not necessarily a global effect of some sub-cortical pacemaker. In fact, if it were a more global effect, it should appear during attention to auditory stimuli as well as visual, an effect which

we studied in this report period.

One of the most fascinating aspects of this project is that it provides us with a method to complement the usual method of recording elcctric potentials at the scalp. These potentials are widely distributed and problems exist in separating sources from each other. While similar problems still beset the intepretation of neuromagnetic field data, there is ample reason to believe that such data are simpler to intepret. In fact, one of the accomplishments of our program to date is the finding that even if a source is a sheet of current dipoles more than 1 cm on a side, the difference in the computed location of the "center of gravity" of the sheet differs by no more than 1 or 2% from the computed location of the source when one assumes that it is a point current dipole at any reasonable depth beneath the scalp. Thus, the error attributable to the assumption of an equivalent current dipole as the source of the observed field is smaller than the experimental error associated with taking such measuremments. Therefore, it is quite reasonable to assume that fields having different sources in widely separated positions in the brain can be resolved by magnetic measures. So one of the problems we are addressing is the differences in locations of sources of phenomena that may be detectable by means of electrodes attached to the scalp. These phenomena include the classic components of the ERP as well as the hypothesized modulation of the background EEG.

To test for the presence of this modulation we employed an

odd ball paradigm in which a frequent visual stimulus was occassionally interrupted by an infrequent (20%) auditory stimulus and, in other blocks of trials, the reverse procedure was used. We measured the ERP betwen an electrode at the vertex or at Pz (this varied across subjects), and one at one mastoid, with the forehead as ground. Also, we measured the magnetic field outside the head in the vicinity of the temporal cortex using our single dcSQUID sensor. We deliberately put off mapping studies, pending the arrival of our multi-sensor array, because it would have been uneconomical to do otherwise. However, it is worth noting that even with the pick up coil positioned at a non-optimum place (not at an extremum of the field) it was possible to retrieve responses to odd balls with only 15-20 trials.

Our data indicate that odd ball stimuli (visual or auditory) usually (though not always) show an elevated P300. One subject in particular did not show an enhancement of P300 for odd ball stimuli. However, for visual stimuli all subjects showed a depression in spontaneous activity in the alpha band immediately following N100, and this depression persisted for about 500 msec when the visual stimulus was an odd ball. If the visual stimulus was frequent, the depression of alpha band activity was present but was quickly restored to baseline after about 100 msec. This was an invariant effect across subjects, regardless of whether or not P300 showed the usual and expected change, depending upon whether the stimulus was an odd ball or not.

Briefly, the procedure used to recover this modulation effect was to store all of the raw EEG data on magnetic tape and then process it, trial by trial, by first reducing all trials to the same length (they were typically 1500 msec between stimuli, but randomized in duration by as much as 500 msec), and then stringing them together so that there was a fundamental frequency with a period equal to the duration of the truncated ISI. Then the fundamental frequency and all of its harmonics were removed from the trials, leaving only the "noise" that was not harmonically related to the stimulus. This noise was then rectified, and the rectified noise was averaged. This average revealed an invariant waveform for odd ball trials and for frequent trials, but they differed in shape and duration. When the "noise" alone was averaged without rectification, there was no response at all, thereby proving that the background activity was indeed modulated by the visual event, for otherwise any residual stimulus-coherent activity would have yielded a response.

It is of some interest to note that only the visual stimulus was capable of eliciting this modulation wave (M-wave). Neither the odd-ball nor the frequent auditory stimulus produced such an effect. However, there was a difference in N100 between auditory and odd ball stimuli, but this is still being investigated. Also, other electrode placements are being tried, since a comparable effect in the auditory system may have a source that differs in orientation and/or location from the location of the set of

neurons that respond to the auditory stimulus per se. In any event, when the "active" electrode was placed near Oz, the M-wave became much stronger (by a factor of 3 or 4) than it was with the active electrode at Pz. This suggests a source in the visual cortex for an attention-related effect on the EEG.

It is quite interesting that the M-wave occurs coincidentally with N100 and is not further modulated by P300 or, when encountered, by N400. Thus, the effect seems to occur independently of P300, and, unlike the latter, it does seem to have a cortical source.

Having verified the presence of an effect on brain events that are not visible in the average ERP but are nonetheless dependent upon attention to these events, we set out to determine if their sources were different from the sources of the usual ERP. This was done by means of magnetic measures. As indicated, these measures were made in the temporal region, and systematic mapping was not yet undertaken. In any event, for both visual and auditory stimuli we detected P300-like phenomena in the temporal region and encountered no reversals in phase in the temporal area. N100 was detected when auditory stimuli were used, but not when visual stimuli were used. Undoubtedly a visual N100 would have been encountered if we had mapped the field in the occipital region. However, the main point is that none of the measures made to date in the temporal region revealed the presence of a magnetic M-wave. We must yet place the pick up coil over the occipital region where we will undoubtedly sense

such an even and locate its source. Tentatively, the M-wave is a modulation of activity of one of the visual areas, and this modulation rewpresents an inhibition of spontaneous activity when visual stimuli are being processed by the brain. If the incoming signal is not "interesting" (as in the case of frequent stimuli), the inhibition is of limited duration. However, if the incoming visual signal is an odd ball ("interesting"), then the visual cortex may well be conserving its capacity to respond by not returning to its normally active state.

2. Magnetic Counteparts to N100

As evidenced by the work of Hillyard and his colleagues, N100 also displays variation in amplitude when cognitive variables are introduced. The magnetic counterpart to N100 was measured when an acoustic stimulus was applied to a subject. The source of this component was located about 1 cm anterior to the tonotopically organized portion of the auditory cortex in 2 subjects. Moreover, the location of this source did not depend upon the frequency content of the tone pip used to evoke the response. Preliminary evidence suggests that this component is contingent upon the presence of virtually any acoustic stimulus (tone pip, click or square-wave change in sound pressure level), but its amplitude depends instead upon the attention given to the event. Work is continuing on this observation. In any event, one relatively firm conclusion is that sensory stimulation is

necessary to the occurrence of N100 (the missing-stimulus paradigm doesn't work) but is not sufficient to account for its magnitude. Cognitive factors are the major contributors to the variance in the magnitude of N100. This also seems to be true of the visual N100, but we lack sufficient data to draw firm conclusions.

3. Magnetic Counterparts to N400

In some of our earlier attempts to produce the P300 phenomenon by means of electrical recording (in the usual fashion), we ran into two problems. The first was an unwanted effect of eye movements, which we had to eliminate by monitoring shifts in eye postion using electrodes attached to the face near the eyes. Once this was accomplished we discovered that another component of the ERP often masked P300. This was a component at N400, which was of a very large amplitude, and P300 could only be observed as a change in the level of negativity of N400. One of our goals was to find a clean electrical response, similar to those studied by other groups, so that we could identify the sources of its components and observe their variability, depending upon stimulus conditions and the state of the subject. We had knowledge of the work of Kutas and of Hillyard on N400. Kutas used either semantic or syntactic anomalies in the context

of a dichotic listening task to produce this effect. We did not expect to encounter it in an odd ball task. Nonetheless, we did. Since it was present, we decided to examine the magnetic response in the temporal area to see if there was reversal of polarity of the response. For if such a reversal occurred over a short distance across the scalp, it would prove that N400 (unlike P300) had a cortical source. In fact, we did find such a reversal of polarity. While the data are still being evaluated, it is possible to say that N100 and N400 have cortical sources, while P300 seems to have a subcortical source. Our data also suggest a subcortical source for N200.

This totally unexpected finding of N400 in an odd ball experiment led us to explore some of the factors that might affect this phenomenon. After testing several hypotheses, we hit upon the idea of varying stimulus intensity. Thus far only two levels of visual and auditory stimulus intensity have been tried. At one level the stimuli are detectable, but are only slightly above threshold. This leads to the obliteration of the N400 in the electrical response (magnetic data have not yet been evaluated). At the second level the stimuli are well above threshold (at least 60 dB). This leads to the presence of N400 in the odd balls, whether they are visual or auditory. Also, these same odd balls produce magnetic N400s having a cortical source.

It is now possible to speculate on the temporal sequence of these components of the ERP. The very earliest components arise

in the primary sensory areas and may or may not reflect some gating effects due to attention. N100 definitely reflects an effect of cortical processing, and its magnitude depends upon attention to the signal being processed. This processing is further reflected in the modulation of EEG activity in at least some portions of the sensory regions of the brain. P200 indicates the arrival of processed information at subcortical nuclei, probably the limbic system. P300 may well indicate the transfer of information between long term and short term memory. The effect of this is the transfer of information back to the cortex (N400) for additional action. This sketchy view of sequencing is consistent with many ideas expressed by others, and it provides no indication of the actual nature of the processing involved. By employing other more complicated paradigms, together with our multi-sensor array, we may well gain a much deeper insight into the processes involved.

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